Application No.: 10/524,197 **Office Action Dated:** July 30, 2007

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1. (Currently Amended) A compound according to the general Formula (I)

the pharmaceutically acceptable acid or base addition salts thereof, the stereochemically isomeric forms thereof **and or** the *N*-oxide form thereof, wherein:

X is CH_2 , $N-R^7$, S or O;

R⁷ is selected from the group of hydrogen, alkyl, Ar, Ar-alkyl, alkylcarbonyl, alkyloxycarbonyl and mono- and di(alkyl)aminocarbonyl;

R¹ and R² are each selected from the group of hydrogen, halo, hydroxy,
-OSO₂H, -OSO₂CH₃, alkyloxy, alkyloxyalkyloxy,
alkyloxyalkyloxyalkyloxy, tetrahydrofuranyloxy, alkylcarbonyloxy,
alkyloxyalkylcarbonyloxy, pyridinylcarbonyloxy,
alkylcarbonyloxyalkyloxy, alkyloxycarbonyloxy, alkenyloxy, alkenyloxy, mono- or di(alkyl)aminoalkyloxy, -N-R¹⁰R¹¹, alkylthio,
Alk and Het.

with the proviso that at least one of R¹ and R² is selected from the group consisting of Alk and Het, wherein

Alk is cyano, CN-OH, CN-oxyalkyl, alkyl, alkyloxyalkyl, alkyloxyalkyloxyalkyl, alkyloxyalkyloxyalkyl, alkylcarbonylalkyl, alkylcarbonyloxyalkyl, alkyloxycarbonylalkyl, Ar-alkyl, Ar-carbonylalkyl, Ar-oxyalkyl, mono- or di(alkyl)aminoalkyl, mono- or di(alkyl)aminocarbonylalkyl, Het-alkyl, formyl, alkylcarbonyl, alkyloxyalkylcarbonyl, mono- or di(alkyl)aminocarbonyl, Ar-carbonyl and Ar-oxycarbonyl;

Ar is phenyl or naphthyl, optionally substituted with one or more halo, cyano, oxo, hydroxy, alkyl, formyl, alkyloxy or amino radicals.

Application No.: 10/524,197 **Office Action Dated:** July 30, 2007

Het is a heterocyclic radical selected from the group consisting of Het¹, Het² and Het³:

Het¹ is an aliphatic monocyclic heterocyclic radical selected from the group consisting of pyrrolidinyl, dioxolyl, imidazolidinyl, pyrrazolidinyl, piperidinyl, dioxyl, morpholinyl, dithianyl, thiomorpholinyl, piperazinyl and tetrahydrofuryl;

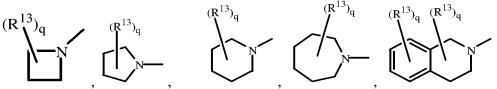
Het² is a semi-aromatic monocyclic heterocyclic radical selected from the group consisting of 2H-pyrrolyl, pyrrolinyl, imidazolinyl and pyrrazolinyl;

Het³ is an aromatic monocyclic heterocyclic radical selected from the group consisting of pyrrolyl, pyrazolyl, imidazolyl, furyl, thienyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, pyridinyl, pyrimidinyl, pyrazinyl, pyridazinyl and triazinyl; or an aromatic bicyclic heterocyclic radical selected from the group consisting of quinolinyl, quinoxalinyl, indolyl, benzimidazolyl, benzoxazolyl, benzisoxazolyl, benzothiazolyl, benzisothiazolyl, benzofuranyl and benzothienyl;

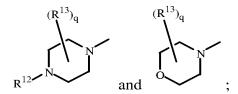
wherein each Het¹, Het² and Het³-radical may optionally be substituted on either a carbon or heteroatom with halo, hydroxy, alkyloxy, alkyl, Ar, Aralkyl, formyl, alkylcarbonyl or pyridinyl;

R¹⁰ and R¹¹ are each, independently from each other, selected from the group consisting of hydrogen, alkyl, Ar, Ar-alkyl, pyrrolidinylalkyl, piperazinylalkyl, piperazinylalkyl, morpholinylalkyl, mono- or di(alkyl)aminoalkyl, alkylcarbonyl, alkenylcarbonyl, Ar-carbonyl, pyridinylcarbonyl, alkyloxycarbonyl, mono- or di(alkyl)aminocarbonyl, mono- or di(alkyl)aminocarbonyl, mono- or di(alkyloxycarbonylalkyl)aminocarbonyl, pyrrolidinylcarbonyl, aminoiminomethyl, alkylaminoiminomethyl, N-benzylpiperazinyliminomethyl, alkylsulphonyl and Ar-sulphonyl; or R¹⁰ and R¹¹ may be taken together and with the N may form a monovalent radical

R¹⁰ and R¹¹ may be taken together and with the N may form a monovalent radica selected from the group of



Application No.: 10/524,197 **Office Action Dated:** July 30, 2007



wherein:

R¹² is selected from the group consisting of hydrogen, alkyl, Ar, Ar-alkyl, Ar-alkenyl, alkylcarbonyl, alkyloxycarbonyl, alkyloxyalkylcarbonyl and monoor di(alkyl)aminocarbonyl;

each ring being optionally substituted with q radicals R¹³, each radical independently from each other selected from the group of alkyl, oxo, Ar, Aralkyl, Ar-alkenyl and alkyloxycarbonyl and q being an integer ranging from 0 to 6; or

 R^1 and R^2 may be taken together to form a bivalent radical - R^1 - R^2 - selected from

the group consisting of -CH₂-CH₂-CH₂-CH₂-, -CH=CH-CH₂-CH₂-,

-CH2-CH2-CH=CH-, -CH2-CH=CH-CH2- and

-CH=CH-CH=CH;

a and b are asymmetric centers;

(CH₂)_m is a straight hydrocarbon chain of m carbon atoms, m being an integer

ranging from 1 to 4;

Pir is a radical according to any one of Formula (IIa), (IIb) or (IIc)

$$(II)$$

$$(R^8)_n$$

$$(B^8)_n$$

$$(B^8)_n$$

$$(B^8)_n$$

$$(B^8)_n$$

$$(B^8)_n$$

$$(C)$$

optionally substituted with n radicals R⁸, wherein:

each R⁸ is independently from each other, selected from the group of hydroxy, amino, nitro, cyano, halo and alkyl;

n is an integer ranging from 0 to 5;

R⁹ is selected from the group consisting of hydrogen, alkyl and formyl;

R³ represents an optionally substituted aromatic homocyclic or heterocyclic ring

Application No.: 10/524,197 **Office Action Dated:** July 30, 2007

system together with an optionally substituted and partially or completely hydrogenated hydrocarbon chain of 1 to 6 atoms long with which said ring system is attached to the Pir radical and of which may contain one or more heteroatoms selected from the group of O, N and S;

alkyl represents a straight or branched saturated hydrocarbon radical having from 1 to 6 carbon atoms or a cyclic saturated hydrocarbon radical having from 3 to 6 carbon atoms, optionally substituted with one or more halo, cyano, oxo, hydroxy, formyl or amino radicals;

alkenyl represents a straight or branched unsatured hydrocarbon radical having one or more double bonds, optionally substituted with one or more halo, cyano, oxo, hydroxy, formyl or amino radicals; and halo is fluoro, chloro, bromo and iodo.

2 (Previously Presented) The compound according to claim 1, wherein R³ is a radical according to any one of Formula (IIIa), (IIIb) or (IIIc)

$$(a) \qquad (b) \qquad (c)$$

wherein:

- d is a single bond while Z is a bivalent radical selected from the group consisting of $-CH_2$ -, -C(=O)-, -CH(OH)-, -C(=N-OH)-, -CH(alkyl)-, -O-, -S-, -S(=O)-, -NH- and -SH-; or d is a double bond while Z is a trivalent radical of formula =CH- or =C(alkyl)-;
- A is a 5- or 6-membered aromatic homocyclic or heterocyclic ring, selected from the group consisting of phenyl, pyranyl, pyridinyl, pyrazinyl, pyrimidinyl, pyridazinyl, thienyl, isothiazolyl, pyrrolyl, imidazolyl, pyrazolyl, furanyl, oxadiazolyl and isoxazolyl;
- p is an integer ranging from 0 to 6; Page 5 of 9

Application No.: 10/524,197 **Office Action Dated:** July 30, 2007

R⁴ is alkyl;

R⁵ is selected from the group consisting of hydrogen, alkyl, Ar, biphenyl, halo and cyano; or

 R^4 and R^5 — may be taken together to form a bivalent radical - R^4 - R^5 - selected from the group consisting of -CH $_2$ -, -CH $_2$ -, -CH $_2$ -CH $_2$ -, -CH=CH-, -O-, -NH-, =N-, -S-, -CH $_2$ N(-alkyl)-, -N(-alkyl)CH $_2$ -, -CH $_2$ NH-, -NHCH $_2$ -, -CH=N-, -N=CH-, -CH $_2$ O- and -OCH $_2$ -;

each R⁶ is independently from each other, selected from the group consisting of hydroxy, amino, nitro, cyano, halo, carboxyl, alkyl, Ar, alkyloxy, Aroxy, alkylcarbonyloxy, alkyloxycarbonyl, alkylthio, mono- and di(alkyl)amino, alkylcarbonylamino, mono- and di(alkyl)aminocarbonyloxy, mono- and di(alkyl)aminoalkyloxy; or

two vicinal radicals R^6 may be taken together to form a bivalent radical $-R^6$ - R^6 -selected from the group consisting of $-CH_2$ - CH_2 -O-, -O- CH_2 - CH_2 -, $-CH_2$ - CH_2 - and $-CH_2$ - CH_2 -, and is selected from the group consisting of hydrogen, alkyl, Ar and Ar-alkyl.

- 3. (Previously Presented) The compound according to claim 2, wherein X=0; m=1; Pir is a radical according to Formula (IIa) wherein n=0; R^3 is a radical according to Formula (IIIb) wherein d is a double bond while Z is a trivalent radical of formula =CH-, A is a phenyl ring, R^4 is alkyl, R^5 and R^{16} are each hydrogen, R^6 is hydrogen or halo and p=1.
- 4. (Previously Presented) The compound according to claim 1 wherein at least one of R¹ and R² is selected from the group consisting of cyano optionally substituted with hydroxy or alkyloxy; alkyl; hydroxyalkyl; aminoalkyl; alkyloxyalkyl; alkyloxyalkyl; alkyloxyalkyl; Ar-oxyalkyl; mono- or di(alkyl)aminoalkyl, the alkyl radicals optionally substituted with hydroxy; mono- or di(alkylcarbonyl)aminoalkyl; mono- or di(alkyl)aminocarbonyl; piperidinylalkyl; morpholinylalkyl; and thienyl optionally substituted with alkylcarbonyl.

Application No.: 10/524,197 **Office Action Dated:** July 30, 2007

5. (Previously Presented) The compound according to claim 1 selected from the group consisting of:

- 8-Methoxy-7-methyl-3-[4-(2-methyl-3-phenyl-allyl)-piperazin-1-ylmethyl]-3a,4-dihydro-3*H*-chromeno[4,3-c]isoxazole;
- {8-Methoxy-3-[4-(2-methyl-3-phenyl-allyl)-piperazin-1-ylmethyl]-3a,4-dihydro-3*H*-chromeno[4,3-c]isoxazol-7-yl}-methanol;
- 7-Methoxymethyl-3-[4-(2-methyl-3-phenyl-allyl)-piperazin-1-ylmethyl]-3a,4-dihydro-*3H*-chromeno[4,3-c]isoxazole;
- 8-Methoxy-7-(2-methoxy-ethoxymethoxymethyl)-3-[4-(2-methyl-3-phenyl-allyl)-piperazin-1-ylmethyl]-3a,4-dihydro-*3H*-chromeno[4,3-c]isoxazole;
- Acetic acid 8-methoxy-3-[4-(2-methyl-3-phenyl-allyl)-piperazin-1-ylmethyl]-3a,4-dihydro-3*H*-chromeno[4,3-c]isoxazol-7-ylmethyl ester;
- 8-Methoxy-3-[4-(2-methyl-3-phenyl-allyl)-piperazin-1-ylmethyl]-7-phenoxymethyl-3a,4-dihydro-*3H*-chromeno[4,3-c]isoxazole;
- 2-(Methyl-{3-[4-(2-methyl-3-phenyl-allyl)-piperazin-1-ylmethyl]-3a,4-dihydro-3*H*-chromeno[4,3-c]isoxazol-7-ylmethyl}-amino)-ethanol;
- 8-Methoxy-3-[4-(2-methyl-3-phenyl-allyl)-piperazin-1-ylmethyl]-7-morpholin-4-ylmethyl-3a,4-dihydro-*3H*-chromeno[4,3-c]isoxazole;
- 3-[4-(2-Methyl-3-phenyl-allyl)-piperazin-1-ylmethyl]-3a,4-dihydro-*3H*-chromeno[4,3-c]isoxazole-7-carbaldehyde oxime;
- 3-[4-(2-Methyl-3-phenyl-allyl)-piperazin-1-ylmethyl]-3a,4-dihydro-*3H*-chromeno[4,3-c]isoxazole-7-carbaldehyde O-methyl-oxime;
- 3-[4-(2-Methyl-3-phenyl-allyl)-piperazin-1-ylmethyl]-3a,4-dihydro-*3H*-chromeno[4,3-c]isoxazole-7-carbonitrile;
- *N*-{3-[4-(2-Methyl-3-phenyl-allyl)-piperazin-1-ylmethyl]-3a,4-dihydro-*3H*-chromeno[4,3-c]isoxazol-7-ylmethyl}-acetamide;
- 8-Methoxy-3-[4-(2-methyl-3-phenyl-allyl)-piperazin-1-ylmethyl]-3a,4-dihydro-3*H*-chromeno[4,3-c]isoxazole-7-carboxylic acid ethylamide;

and

- 1-(5-{8-Methoxy-3-[4-(2-methyl-3-phenyl-allyl)-piperazin-1-ylmethyl]-3a,4-dihydro-3*H*-chromeno[4,3-c]isoxazol-7-yl}-thiophen-2-yl)-ethanone.
- 6. (Original) A compound which is degraded *in vivo* to yield a compound according to claim 1.

Application No.: 10/524,197 **Office Action Dated:** July 30, 2007

- 7. (Canceled)
- 8. (Canceled)
- 9. (Previously Presented) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and, as active ingredient a therapeutically effective amount of a compound according to claim 1.
- 10. (Canceled).
- 11. (Previously Presented) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and, as active ingredient a therapeutically effective amount of a compound according to claim 1 and one or more other compounds selected from the group consisting of antidepressants, anxiolytics and antipsychotics and anti-Parkinson's disease drugs.
- 12. (Canceled).
- 13.-16. (Canceled).